Testimony
Before the Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
United States House of Representatives

Policies of the Intramural Research Program at the National Institutes of Health

Statement of
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Good morning Mr. Chairman, Mr. Stupak, and Members of the Subcommittee. I am Dr. Michael Gottesman, the Deputy Director for Intramural Research at the National Institutes of Health (NIH), an agency within the U.S. Department of Health and Human Services (HHS). I am responsible for oversight and coordination of intramural research, training, and technology transfer activities conducted within the laboratories of the 22 intramural programs of the NIH. The intramural program represents about 10 percent of the total NIH budget, or $2.8 billion in Fiscal Year 2006. Our 6000 intramural scientists work in an environment where creativity is encouraged and cutting edge research is the norm.

The intramural research program provides unique opportunities and resources to encourage important high-risk, high impact scientific inquiries that may be difficult to pursue in the private sector or academia. Intramural laboratories are regularly subjected to rigorous outside reviews.

The NIH Clinical Center is the focal point of the intramural enterprise, where laboratory scientists and clinicians work in close physical and intellectual proximity, providing a unique cauldron for translational and clinical research, with the cost of patient participation covered by the NIH budget. The first chemotherapeutic cures for childhood leukemia and Hodgkin's disease, and the first use of AZT to treat AIDS, resulted from research done at the Clinical Center, the largest research hospital in the country. Of the 19 scientists with medical degrees who have won Nobel Prizes in Medicine in the past 20 years, nine were trained in the intramural program at NIH.

The NIH intramural research program could not succeed – nor could any scientific endeavor – without collaborative interactions between our scientists and investigators in academic research

institutions and private industry in the course of their official work. Such collaborations are encouraged. Without them, the pathway to discovery would likely be slowed by innumerable obstacles and many of our greatest research achievements might not have occurred.

Of course, policies intended to facilitate collaborations between federal and private sector researchers must be firmly grounded in ethical principles. The NIH's leadership was reminded of the importance of this requirement two years ago by this Subcommittee's investigation of consulting arrangements between intramural scientists and companies in the pharmaceutical and biotechnology industries. Your oversight review prompted NIH and HHS to revisit and dramatically strengthen ethics regulations in 2005.

New HHS regulations addressed vulnerabilities in the NIH's ethics system by completely banning all personal or outside consulting by NIH scientists with pharmaceutical and biotechnology companies. Private outside consulting on subjects that are the same as or similar to an employee's official duties has always been prohibited, even under previous regulations. The events under consideration at today's hearing occurred before these new regulations were issued. It is a sensitive matter that is still the subject of ongoing review.

The events are connected to research on Alzheimer's disease, specifically attempts to identify biomarkers that identify the early presence of the disease. This research is one of the most important areas of investigation regarding Alzheimer's disease and should be pursued with vigor. But the quest for biomarkers by NIH must be conducted according to Federal rules pertaining to human subjects protection, intellectual property, and conflicts of interest.

As I understand it, the Subcommittee has specific concerns about the transfer of human biological samples from NIH to the private sector in connection with a consulting arrangement. NIH shares these concerns.

First and foremost, we want to know if important biological samples were transmitted without adequate controls and if human subject protection requirements were met.

Second, we want to be sure that our internal controls on biological samples support the application and enforcement of all requirements, including the regulation governing outside or personal activities.

Regardless of the outcome of the multiple reviews concerning this matter, I want to be perfectly clear about NIH's position. Any attempt to illegally profit from official research activities, especially where human biological samples are involved, is totally unacceptable. Engaging in such an activity is a violation of NIH's core ethical principles, past and present. We can not tolerate such behavior.

I am told that the material in question – spinal fluid taken from Alzheimer's disease patients – was provided by a NIH intramural scientist to a pharmaceutical company. This transfer of human tissue samples has raised numerous issues and concerns, including the adequate protection of the rights of individuals who participate in clinical trials, alleged conflict of interest, and intellectual property issues. These areas of oversight involve complex regulations and interactions that need to be clarified.

With this principle in mind, on August 25, 2005, HHS, with the concurrence of the Office of Government Ethics, published a final rule governing standards of ethical conduct for NIH employees. The new regulation contains the following additional provisions:

- All NIH employees are now prohibited from engaging in outside employment with pharmaceutical companies and biotechnology companies.
- The extent to which the most senior NIH employees may hold certain types of stock and other financial interests is severely limited.
- The number of employees required to disclose financial interests is significantly expanded.

In addition to the reforms implemented in our ethics program, we are enhancing policies pertaining to the handling of human tissue samples and related intellectual property. While sharing such materials facilitates and accelerates the scientific process, it is also clear that additional protections must be in place when scientists share human tissue samples, such as blood, serum, or as in this case, cerebrospinal fluid. Accordingly, after reviewing our policies and procedures regarding the transfer of such materials, we determined that further clarification is necessary. In order that NIH employees understand that formal mechanisms such as Material Transfer Agreements (MTAs) are required when human research materials are transferred, we are taking the following steps:

- NIH will provide additional guidance to investigators on the different mechanisms available for entering into collaborations and transferring materials outside of the NIH. While we thought that the current rules were clear to most scientists, we think it is

necessary to clarify that a MTA should be used when transferring materials. Scientists should use research collaborative agreements, or Cooperative Research and Development Agreements (CRADAs), when entering into research collaborations with industry.

- NIH will require that all transfers of samples derived from human subjects must involve a written mechanism – MTA, CRADA, letter of collaboration, or other agreement. Such agreements must be in writing to ensure compliance with all requirements regarding human subjects protections. Further, the use of written mechanisms will permit NIH to track the sharing of clinical samples with outside entities, and monitor compliance with the policy.
- NIH will clarify that in cases involving the transfer of material derived from human subjects, all such written agreements must be accompanied by more rigorous checks and balances, including the review and approval by senior leadership at the relevant Institute.
- NIH has initiated a comprehensive review of policies across NIH involving MTAs to determine if additional requirements are necessary in the case of MTAs that do not involve the transfer of material derived from human participants. NIH policy requires the widespread dissemination of research tools. It is not clear, however, that such enhanced protections should be required for all materials, such as laboratory-produced DNA samples, cell lines, and antibodies, whose main function is to accelerate research. A further analysis is necessary to inform policy development in this area.

NIH has also reviewed its policies governing the use of stored human tissue samples. Stored human tissue samples, if identifiable by codes or other identifiers, are considered "human subjects" under applicable Federal regulations. The intramural research program's human research protection program functions under a Federal-Wide Assurance (FWA) with the HHS

Office for Human Research Protections (OHRP). Its FWA commits the intramural program to conduct its human subjects research activities consistent with acceptable ethical principles and in compliance with 45 CFR part 46, the regulation governing the protection of human subjects in research. I am responsible for implementing the FWA, and the Office of Human Subjects Research (OHSR) within the Office of Intramural Research serves this purpose.

Research uses of previously collected and stored human samples, when intramural research program investigators can personally identify the sources, must be prospectively reviewed and approved by an Institutional Review Board (IRB). IRBs are charged by federal regulation (45 CFR part 46) with reviewing research protocols from the vantage point of protecting the rights and safeguarding the welfare of the research participants. When reviewing a proposed new research use of stored samples, an IRB will consider the original research use and carefully consider the informed consent document in order to determine if the new use is consistent with the original protocol. If the research is subject to regulation by the Food and Drug Administration (FDA) (for example, if an investigational diagnostic test is being studied), then the IRB would also apply FDA regulations. We believe the process for reviewing new uses of stored samples must be clear and rigorous. In order to assure that all NIH intramural research program researchers understand the requirements for the research use of stored samples, the following steps have been or will be taken:

- A memorandum has been sent to all intramural clinical researchers, clinical directors, and scientific directors clarifying the oversight requirements for the collection and research use of human samples, data and specimens.

- The Clinical Center's Medical Executive Committee implemented procedures to assure that all Clinical Center protocols receive continuing NIH IRB review and approval as long as research analyses using coded samples continues.
- NIH will modify its standard MTA form to include language indicating that the transfer of either coded or identifiable samples has been reviewed by an IRB or is exempt from IRB review pursuant to 45 CFR part 46 as determined by OHSR. This step will assist technology transfer staff in determining whether the scientist has adhered to human subjects requirements.
- All research protocols in which intramural researchers intend to collect and store human samples, specimens, or data must include a description of the intended use of the samples; how the samples will be tracked; how they will be stored; what will happen to the samples at the completion of the protocol; what circumstances would prompt the investigator to report to the IRB loss or destruction of samples, and any proposed future use (i.e., use after termination of the protocol). Consent documents must include relevant language. While we cannot anticipate all prospective uses, we want to ensure that research participants have as much information as possible on how their own material will be maintained and used.

These steps will help ensure that investigators fully understand NIH requirements for the research use of previously collected, stored human samples, and that proposals for such uses must be approved by an IRB and by OHSR.

Science is an ongoing process that requires constant review and adaptation. The same is true for NIH's programs that manage the research enterprise. Many of our adaptations result from

internal review. Some ensue from external oversight, such as the work of this Subcommittee. In either case, NIH's leadership understands we must be responsive.

Sometimes the problems identified by internal and external oversight are systemic, but sometimes they result from individual behavior. To the extent NIH identifies systemic issues, we will take appropriate action. In the case of individual misconduct, we will seek remediation, including dismissal, where warranted.

Thank you for this opportunity, Mr. Chairman. I will be pleased to answer your questions.